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## The Diabetes Dilemma for Statin Users

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We're overdosing on [cholesterol](#)-lowering statins, and the consequence could be a sharp increase in the incidence of [Type 2 diabetes](#).

This past week, the Food and Drug Administration raised questions about the side effects of these drugs and developed new labels for these medications that will now warn of the risk of [diabetes](#) and [memory loss](#). The announcement said the risk was "small" and should not materially affect the use of these medications. The data are somewhat ambiguous for memory loss. But the magnitude of the problem for diabetes becomes much more apparent with careful examination of the data from large clinical trials.

[Statins](#) have been available since the 1980s but their risk of inducing diabetes did not surface for nearly 20 years. When all the data available from multiple studies was pooled in 2010 for more than 91,000 patients randomly assigned to be treated with a statin or a sugar pill (placebo), the risk of developing diabetes with any statin was one in every 255 patients treated. But this figure is misleading since it includes weaker statins like Pravachol and Mevacor — which were introduced earlier and do not carry any clear-cut risk. It is only with the more potent statins — [Zocor](#) (now known as simvastatin), [Lipitor](#) (atorvastatin) and [Crestor](#) (rosuvastatin) — particularly at higher doses, that the risk of diabetes shows up. The cause and effect was unequivocal because the multiple large

trials of the more potent statins had a consistent excess of diabetes.

For those statins, the higher the dose, the more diabetes, though we don't have enough data yet to say with precision at which dose excess diabetes showed up for each drug. What we do know is that diabetes showed up. The numbers increase to one in 167 for patients taking 20 milligrams of Crestor, and up to one in 125 for intensive statin treatments involving drug strategies to markedly lower cholesterol levels. Let's just round this off and say that one in every 200 patients treated with any of the three most potent statins will get the side effect of diabetes. That's quite a conservative number because diabetes was not even being carefully looked for in most of the trials. And we have data for only 5 years of treatment; it might be worse with longer statin therapy.

More than 20 million Americans take statins. That would equate to 100,000 new statin-induced diabetics. Not a good thing for the public health and certainly not good for the individual affected with a new serious chronic illness.

If there were a major suppression of heart attacks or strokes or deaths, that might be justified. But in patients who have never had heart disease and are taking statins to lower their risk (so-called primary prevention), the reduction of heart attacks and other major events is only 2 per 100. And we don't know who the 2 per 100 patients are who benefit or the one per 200 who will get diabetes! Moreover, the margin of benefit to risk is quite narrow.

What should people who are taking statins do? If they are prescribed for someone who has already had heart disease or a stroke, the benefit is overriding — no changes are suggested. But in the vast majority of people who take statins — those who have never had any heart disease — there should be a careful review of whether the statin is necessary, in light of the risk of diabetes and the relatively small benefit that can be

derived. Beyond that, a dose reduction or use of a less potent statin should be considered on an individual basis.

We need to find out why statins cause diabetes and, ideally, through genomics we could determine who is at risk for this important side effect. But to date nothing has been done to sort this out — despite the fact that the market for statins is well over \$20 billion per year. There are thousands of blood samples sitting in company freezers around the world that could potentially provide the answers.

The announcement, medication label change and health advisory by the F.D.A. were long overdue, and have brought this important public health issue to light. The information that we have does not support that this is a “small” problem unless one considers more than 100,000 new diabetics insignificant. The problem of statin-induced diabetes cannot be underplayed while the country is being overdosed.

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